

C1
This object is achieved by the invention by providing new, isolated or recombinant, antimicrobial peptides thrombocidin-1 (TC-1) (SEQ ID NO: 12) and thrombocidin-2 (TC-2) (SEQ ID NO: 6) or variants thereof, such as TC-1^{*}, (SEQ ID NO: 3), which comprise, at least in part, the sequence as shown in figure 1 and have broad antimicrobial activity. These peptides, or variants thereof, thus may be effectively used as antibiotics in the treatment of several infectious diseases. These peptides can be isolated from both human and animal tissue.

On page 3, please delete and replace the current version of the first full paragraph starting on line 10 with the following replacement paragraph. A marked-up version of the replacement paragraph is attached as a separate sheet.

C2
The new peptides of the invention appear to be derivatives of NAP-2 and CTAP-III. NAP-2 itself is a N-terminal cleavage product of CTAP-III. TC-1 has been shown to be a mixture of C-terminal truncation products of NAP-2, of which the 7436 Da peptide, lacking two C-terminal amino acids, is the main component (referred to as variant TC-1^{*}; (SEQ ID NO: 3), figure 1, table 1). A form of NAP-2 with an additional N-terminal tyrosine was also present as a minor component. TC-2 (SEQ ID NO: 2) has been identified as a C-terminal truncation product of CTAP-III (SEQ ID NO: 1) lacking the last two C-terminal amino acids, with a molecular weight of 9100 (figure 1A, table 1). Thrombocidins identified thus far are indicated in fig. 1A, together with the known sequences of CTAP-III (SEQ ID NO: 1) and NAP-2 (SEQ ID NO: 13) (fig. 1).

On page 5, please delete and replace the current version of the third full paragraph starting on line 21 with the following replacement paragraph. A marked-up version of the replacement paragraph is attached as a separate sheet.

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The present invention thus provides new, isolated or recombinantly prepared peptides TC-1 (SEQ ID NO: 12) and TC-2 (SEQ ID NO: 6), or variants thereof, such as TC-1* (SEQ ID NO: 3) (fig 1 and 2), which exhibit antibacterial and/or antifungal activity and can be used in the treatment of infections in humans and animals. Furthermore, the peptides, or variants thereof, of the present invention can be used for the preparation of a medicament for the treatment of bacterial and/or fungal infections.

On page 8, please delete and replace the current version of the paragraph starting on line 37 and bridging page 9, ending on line 11, with the following replacement paragraph. A marked-up version of the replacement paragraph is attached as a separate sheet.

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ES spectroscopy of TC-2 (fig 7b) yielded a molecular weight of $9100,5 \pm 1,3$. This value was confirmed by MALDI-tof spectroscopy. In addition to TC-2, only one minor contamination was present (10081 Da, fig 9). Partial sequencing of TC-2 indicated that the N-terminus of TC-2 is identical to that of CTAP-III. Based on the mass-spectrometrical data (figs 7b and 9) however, it appears that the mass found experimentally was smaller than the mass of CTAP-III (table 1). This can be explained by assuming that TC-2 is truncated C-terminally and misses 2 amino acids compared to CTAP-III. Thrombocidins identified thus far are indicated in fig 1, together with the sequences of CTAP-III (SEQ ID NO: 1) and NAP-2 (SEQ ID NO: 13).

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On page 10, please delete and replace the current version of the paragraph entitled EXAMPLE 2 that starts on line 1 and bridges page 11, ending on line 6, with the following replacement paragraph. Pursuant to 37 C.F.R. § 1.121, the following is a clean version of the replacement paragraph. A marked-up version of the replacement paragraph is attached on a separate sheet. Please note that both the marked-up version and the clean version contain underlining that is to be retained and does not constitute an amendment.

EXAMPLE 2

Production of recombinant (r) CTAP-III, rNAP-2, rTC-1, rTC-1* and rTC-2.

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From a human bone marrow CDNA library (Clontech, Palo Alto, USA) DNA coding for PBP was amplified in a PCR. 5' TATAGGATCCATGAGCCTCAGACTTGATAC CACC-3' (SEQ ID NO: 7) and 5' TATAGGATCCTCAATCAGCAGATTCATCAC CTGCCAAT-3' (SEQ ID NO: 8) were used as forward and reverse primers, respectively. BamHI restriction sites (underlined) were added to allow cloning in a suitable vector. A stop sequence (boldface) was included to allow proper transcription termination at the stage of protein expression. This PCR was performed using 2 ng of template DNA and Pfu DNA polymerase, which has proofreading capacity. The resulting product was of the expected size (400 bp). This product served as a template in a second PCR to produce the coding DNA of TC-1 (SEQ ID NO: 12), TC-2, CTAP-III (SEQ ID NO: 1), NAP-2 (SEQ ID NO: 13) and TC-1* (SEQ ID NO: 3), a variant of TC-1 which lacks two C-terminal amino acids (Ala-Asp) and carries two additional N-terminal amino acids (Ala-Glu) (fig 2). These PCR products were cloned into expression vectors. For CTAP-III, NAP-2 and TC-1 the reverse primer was the same as the reverse primer described above. The forward primers were as follows:

for CTAP-III and TC-2:

5' GTGTAACATATGAACTTGGCGAAAGGCAAAGAG-3' (SEQ ID NO: 9);

for NAP-2 and TC-1*;

5' GTGTAACATATGTATGCTGAACTCCGCTGCATG 3' (SEQ ID NO: 10);

and for TC-1:

5' GTGTAACATATGTATCTCCGCTGCATGTGTATAAAG-3' (SEQ ID NO: 11).